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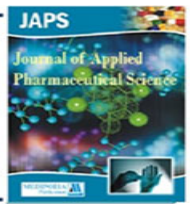

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Eco friendly spectrophotometric method for quantitative estimation of lomefloxacin using hydrotropic approach

Ruchi Jain, Vaibhav Jain, Nilesh Jain, Deepak Kumar Jain and Surendra Jain

Ruchi Jain
Suresh Gyan Vihar University, Mahal, Jagatpura Jaipur, India.

Vaibhav Jain, Nilesh Jain, Surendra Jain
Sagar Institute of Research and Technology- Pharmacy, SIRT-Campus, Ayodhya By-Pass Road, Bhopal, M.P-462041, India.

Deepak Kumar Jain
Truba Institute of Pharmacy, Karond Gandhi Nagar Bypass Road, Bhopal, M.P-462038, India.

For Correspondence
Mrs. Ruchi Jain
Sagar Institute of Research and Technology-Pharmacy, Bypass Road, Bhopal – 462036, India.
Mobile. No-+919425184145

ABSTRACT

The present work describes a novel, accurate, sensitive and economic safe spectrophotometric method was developed by application of hydrotropy, using 8 M Urea solution as hydrotropic solubilizing agent, for the quantitative determination of poorly water-soluble lomefloxacin HCl in tablet dosage form. There were more than 43 times enhancements in the solubility of lomefloxacin HCl increases in hydrotropic solution as compared to solubilities in distilled water. Lomefloxacin HCl shows maximum absorbance at 281 nm. Urea and other tablets excipents did not show any absorbance above 230 nm, and thus no interference in the estimation was seen. Lomefloxacin HCl was obeyed Beer,s law in the concentration range of 5 to 25µg/ml (r2= 0.9998) in hydrotropic solvent with mean recovery ranging from 98.03±0.65 to 98.59±0.32%. Proposed method is new, simple, economic, safe, rapid, accurate and reproducible. The developed methods were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values. The method can be used for routine analysis in both research laboratories, and pharmaceutical and chemical industries to analyze the drugs without the use of organic solvents thus make the environment eco-friendly.

Keywords: Lomefloxacin HCl, Urea, Spectrophotometry, Eco-friendly, Hydrotropic.

INTRODUCTION

Lomefloxacin (LM) 1-ethyl-6,8-difluoro-7-(3-methylpiperazin-1-yl)-4-oxo-1,4 dihydro quinoline -3- carboxylic acid, HCl (Fig-1) is a fluoroquinolone antibiotic used to treat bacterial infections including bronchitis and urinary tract infections.(Brunton *et al.*, 1996: Klimberg *et al.*, 1998). It is also used to prevent urinary tract infections prior to surgery. It is an INN drug and as such it has not been yet included in the BP or USP. Several types of analytical methods have been reported for the analysis of lomefloxacin hydrochloride in plasma and pharmaceuticals formulations, like UVspectroscopy, (Gomes *et al.*, 2005, Suhagia *et al.*, 2006; Amin *et al.*, 2008), HPLC, (Garcia *et al.*, 2001, Zendelovaska *et al.*, 2005, Carlucci *et al.*, 1993, Shibl *et al.*, 1991, Tozo *et al.*, 2006; Atef *et al.*, 2006), polarography, (Song *et al.*, 2001), voltammetry, (Zhang et al., 2003), capillary electrophoresis, (Kowalski *et al.*, 2008), spectrofluorometry. (Abdalla *et al.*, 2008).

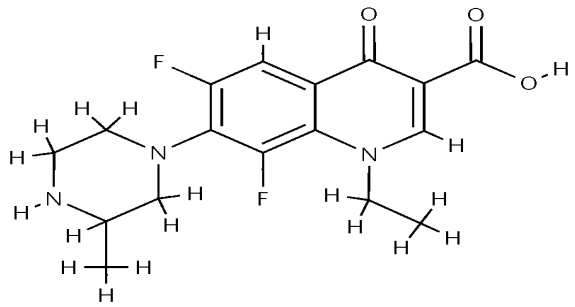

Fig.1: Chemical structure of lomefloxacin.

As the enviormental pollution it is nessecery to perclude the use of organic solvents for analysis of drug. Maheshwari et al (Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2005, Maheshwari *et al.,* 2005, Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2005, Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2005, Maheshwari *et al.,* 2006, Maheshwari *et al.,* 2007, Maheshwari *et al.,* 2006; Maheshwari *et al.,* 2006)and Jain et al (Jain *et al.,* 2010, Jain *et al.,* 2010, Jain *et al.,* 2011; Jain *et al.,* 2011) has analyzed various poorly water soluble drugs using hydrotropic solubilization phenomenon. The term "hydrotropy" has been used to designate the increase in aqueous solubility of various poorly water-soluble compounds due to the presence of a large amount of additives. Sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate are the most common examples of hydrotropic agents utilized to increase the water solubility. Hydrotropic solution may be a proper choice to preclude the use of organic solvents. The purpose of the present study thus was to develop ecofriendly spectrophotometric method for the analysis of lomefloxacin in pharmaceutical dosage form which would be simple, rapid, cost-effective, reproducible and can also be used for quantitative estimation in research laboratory for research purpose and in pharmaceutical industries for routine analysis of lomefloxacin.

MATERIALS AND METHODS

Instrument

The proposed work was carried out on a shimadzu UV-Visible spectrophotometer (model uv-1700 series], which possesses a double beam double detector configuration with matched 1 cm quarts cells.

Chemicals and solvent

Standard lomefloxacin hydrochloride (potency 99.99%] was a kind gift from Intas Pharma Ltd. Mumbai. It was collected in an air tight vial, stored in a cool & dry place and was used without further purification. Urea obtained from Merck Chemical Division, Mumbai. Commercial tablets of lomefloxacin-400 mg (Intas Pharma) were procured from the local drug market.

Preliminary solubility studies

Solubility of drug was determined at 25±1°C. An excess amount of drug was added to a screw capped 25 ml of volumetric flask containing different aqueous systems viz distilled water, buffer of pH 6.4, buffer of pH 8.2, and 8M urea solution. The volumetric flasks were shaken mechanically for 12 hrs at 25±1°C in a mechanical shaker. These solutions were allowed to equilibrate for next 24 hrs and then centrifuged for 5 min at 2000 rpm. The supernatant liquid was taken for appropriate dilution after filtered through Whatmann filter paper #41 and analyzed spectrophotometrically against corresponding solvent blank. After analysis, it was found that the enhancement in the solubility of lomefloxacin was found to be more than and 43 folds in 8M urea solution as compared to solubility studies in other solvents. This enhancement of solubility is due to the hydrotropic solubilization phenomenon.

Determination of wavelength of maximum absorption (λ_{max})

The stock solution (100 µg/ml) was diluted to 10 times to give a solution of 10µg/ml and 5mL of this solution was taken in a cuvette and scanned from 200 to 400 nm with Shimadzu Double Beam UV-VIS 1700Spectrophotometer. The distilled water was used as the blank. Lomefloxacin was found to absorb maximum radiation at 281 nm and spectra of lomefloxacin were shown in Fig-2.

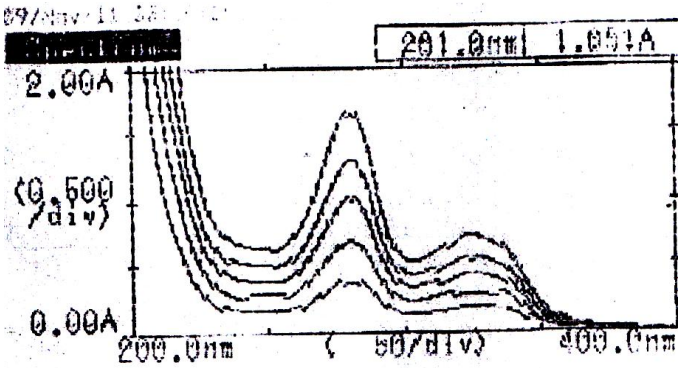

Fig. 2: UV Spectra of lomefloxacin.

Preparation of calibration curve

Accurately weighed 100 mg of the lomefloxacin drug sample were transferred in to 100 ml volumetric flask containing 10 ml of 8 M urea solution and diluted up to 100 ml with distilled water. The standard solution (1000 µg/ml) was further diluted with distilled water to obtain 5, 10, 15, 20 and 25 µg /ml. Likewise the dilution ranging from 05-25 µg/ml were prepared in urea. Detection wavelength was selected for lomefloxacin was 281 nm. Absorbance was noted against distilled water as blank. Calibration curve was plotted between concentration verses wavelength. Spectral data shown in Table-1 and calibration curve in Fig-3.

Table. 1: Optical Characteristic and Linearity Data of Lomefloxacin.

S.No.	PARAMETER	LOMEFLOXACIN
1	Working λ	281nm
2	Beer's law limit (µg/ml)	5-25
3	Correlation Coefficient (r2)*	0.9998
4	Slope (m)*	0.7290
5	Intercept (c)*	0.0013
6	Number of samples (n)	15

*Average of five determination

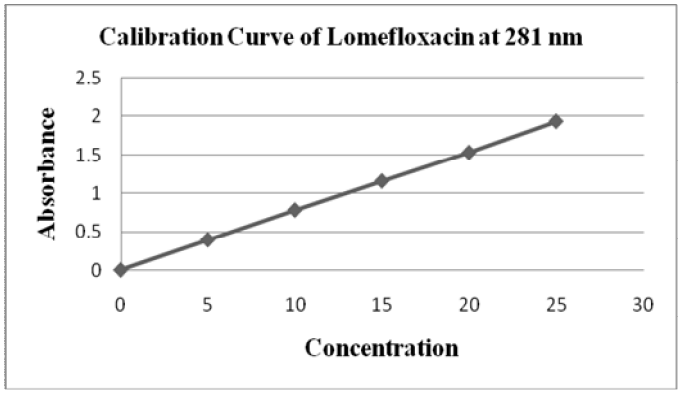

Fig. 3: Calibration Curve of lomefloxacin at 281nm.

Analysis of tablet formulation

Marketed formulation lomefloxacin -400 mg (Intas Pharma) were selected for tablet analysis. Twenty tablets of formulation were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 10 mg of lomefloxacin was transferred to 100 ml of volumetric flask containing 10 ml of 8 M urea solution. The flask was sonicate for about 10 min to solubilize the drug and the volume was make up to mark with distilled water. The solution was filtered through Whatmann filter paper No 41. The filtrate was diluted appropriately with distilled water and was analyzed on UV spectrophotometer against distilled water as blank. Drug content of tablet formulation were calculated using calibration curve & results of statistical data shown in Table-2**.**

Validation

Linearity & Range

The linearity of calibration curves (Absorbance Vs concentration) in pure solution was checked over the concentration ranges of about 05-25 µg/ml of lomefloxacin.

Accuracy

To check the degree of accuracy of the method, recovery studies were performed in triplicate by standard addition method at 80%, 100% and 120%. In preanalyzed tablet solution, a definite amount of drug was added and then its recovery was studied. These studies were performed in by adding fixed amount of pure drug solution to the final dilution while varying the concentration of tablet sample solution in the final dilution. The percentage recovery and percentage relative standard deviation of the recovery were calculated and shown in Table-3.

Precision

To evaluate precision at different parameter like repeatability, intermediate precision and reproducibility, five dilutions in three replicates were analyzed in same day, in two different days and by two analysts for day to day and analyst to analyst variation. The %RSD values for Intraday and Interday precision were < 2%, indicating that the method was sufficiently precise. The results were shown in the Table-4.

RESULTS AND DISCUSSION

Based on the solubility and stability and spectral characteristics of the drug, 8 M urea was selected as hydrotropic agent. Lomefloxacin after solubilized in the selected hydrotropic agent was scanned in spectrum mode and 281nm was selected as wavelength for estimation considering the reproducibility and variability of the obtained result. The developed method was found to be linear in the range of 5 to 25µg/ml with correlation coefficient (r2) of 0.9998 in urea. The mean Percent label claims of tablets of lomefloxacin in formulation estimated by the proposed method were found to be 97.33 to 99.32 in urea. These values are close to 100, indicating the accuracy of the proposed analytical method. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method table 2. The values of mean percent recoveries were also found to be ranging from 98.03±0.65 to 98.59±0.32% in urea. Also the values of standard deviation, percent coefficient of variation and standard error were satisfactorily low table 3. Result of precision at different level were found be within acceptable limits (RSD ‹ 2) table 4.

Table. 2: Results and Statistical Parameters for Tablet Analysis.

DRUG	Label Claim (in mg)	Amount Found (in mg)	% MEAN*	S.D.*	%COV*	STD. ERROR*
Lomefloxacin	400	397.19	99.32	0.12	0.12	0.29
Lomefloxacin	400	389.31	97.33	0.93	0.96	0.77
Lomefloxacin	400	394.04	98.51	0.67	0.68	0.61

*Average of five determination

Table. 3: Results of Recovery Studies on Marketed Formulations.

Drug	QC Conc (µg/ml)	Recovery Level % (Amount Drug Added)	Amount of Drug Found (Mean±SD)*	% RSD
Lomefloxacin	10	80	99.50±0.73	0.73
		100	98.67±0.93	0.94
		120	99.22±1.02	1.03
Lomefloxacin	20	80	98.59±0.32	0.33
		100	98.03±0.65	0.66
		120	98.82±0.85	0.87

*Average of five determination

Table. 4: Results of Precision.

PARAMETER		Mean±SD*	%RSD
Precision (Mean±SD)*	Repeatability	98.72±1.28	1.30
	Intermediate Precision		
	Day to Day	97.98±1.02	1.04
	Analyst to Analyst	98.49±0.12	0.12
	Reproducibility	99.91±0.72	0.72

*Average of five determination

CONCLUSION

It was, thus, concluded that the proposed method is new, simple, cost effective, accurately, precise, safe and free from pollution and can be successfully employed in the routine analysis of lomefloxacin in bulk drug and tablet dosage forms. Presence of hydrotropic agent do not shows any significant interference in the spectrophotometric assay thus further confirming the applicability and reproducibility of the developed method.

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